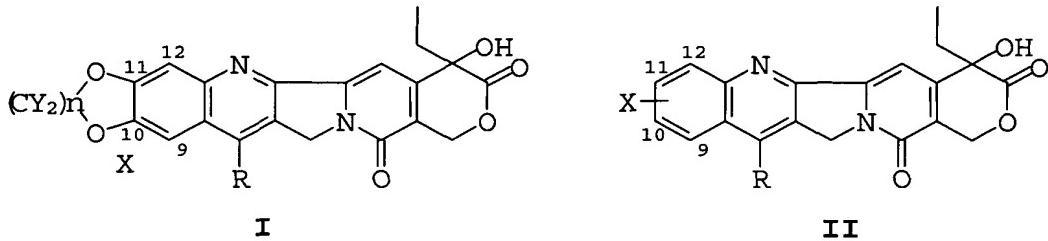


WHAT IS CLAIMED AS NEW AND DESIRED TO BE SECURED BY LETTERS

PATENT OF THE UNITED STATES IS:

1. A method for the preparation of 7-substituted camptothecin compounds of formula (I) or (II):



where

X is H, NH₂, H, F, Cl, Br, O-C₁₋₆ alkyl, S-C₁₋₆ alkyl, NH-C₁₋₆ alkyl, N(C₁₋₆ alkyl)₂, or C₁₋₈ alkyl,

or X is -Z-(CH₂)_a-N-(C₁₋₆ alkyl)₂ wherein Z is selected from the group consisting of O, NH and S, and a is an integer of 2 or 3,

or X is -CH₂NR²R³, where (a) R² and R³ are, independently, hydrogen, C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₃₋₇ cycloalkyl-C₁₋₆ alkyl, C₂₋₆ alkenyl, C₁₋₆ alkoxy-C₁₋₆ COR⁴ where R⁴ is hydrogen, C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₃₋₇ cycloalkyl-C₁₋₆ alkyl, C₂₋₆ alkenyl, C₁₋₆ alkoxy, C₁₋₆ alkoxy-C₁₋₆ alkyl, or (b) R² and R³ taken together with the nitrogen atom to which they are attached form a saturated 3-7 membered heterocyclic ring which may contain a O, S or NR⁵ group, where R⁵ is hydrogen, C₁₋₆ alkyl, alkyl, aryl, aryl substituted with one or more groups selected from the group consisting of C₁₋₆ alkyl, amino, C₁₋₆ alkylamino, C₁₋₆ alkoxy, C₁₋₆ alkoxy-C₁₋₆ alkyl C₁₋₆ alkyl C₁₋₆ alkoxy, aryl, and aryl substituted with one or more C₁₋₆ alkyl, or C₁₋₆ alkoxy-C₁₋₆ alkyl groups;

R is C₁₋₃₀ alkyl, substituted C₁₋₃₀ alkyl, C₁₋₃₀ alkenyl, substituted C₁₋₃₀ alkenyl, C₁₋₃₀ alkynyl, substituted , C₁₋₃₀ alkynyl, C₃₋₃₀ cycloalkyl, substituted C₃₋₃₀ cycloalkyl, C₆₋₁₈ aryl,

substituted C₆₋₁₈ aryl, C₆₋₁₈ aryalkyl, (C₁₋₃₀ alkyl)₃ silyl or (C₁₋₃₀ alkyl)₃ silyl C₁₋₃₀ alkyl,

Y is independently H or F,

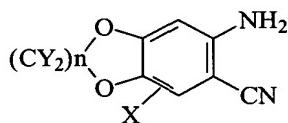
and

n is an integer of 1 or 2,

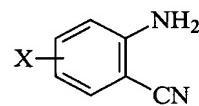
and salts thereof

comprising:

- i) reacting an ortho amino cyano aromatic compound of formula (III) or (IV)



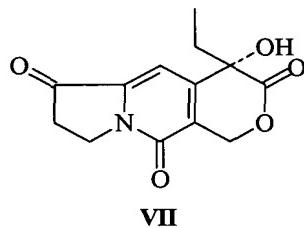
III



IV

with an organometallic reagent R -M and

- ii) condensing a resulting product with a 20(S)tricyclic ketone of formula (VII)



VII

2. The method of claim 1, wherein R-M is selected from the group consisting of cyclohexylmagnesium halide, allyl magnesium halide, vinyl magnesium halide, ethyl magnesium halide, 4-fluorophenylmagnesium halide, isopropenyl magnesium halide, isopropyl magnesium halide, methyl magnesium halide, ethynyl magnesium halide, cyclopentyl magnesium halide, phenyl magnesium halide, benzyl magnesium halide, propyl magnesium halide, 1-propynyl magnesium halide, *p*-tolyl magnesium halide, *o*-tolyl magnesium halide, 1-trimethylsilylmethyl magnesium halide, hexyl magnesium halide, 2-thiophenyl magnesium halide, 4-dimethylaminophenyl magnesium halide, 4-chloro 1-but enyl

2-magnesium halide, *p*-methoxylbenzyl magnesium halide, methoxymethyl magnesiumhalide, and *p*-chloro phenylmagnesium halide, *n*-butyl magnesium halide, *s*-butyl magnesium halide, *t*-butyl magnesium halide and p-trifluoromethylphenylmagnesium halide.

3. The method of claim 2, wherein said ortho amino cyano aromatic compound is a compound of formula (III), R-M is *n*-butyl magnesium halide, and R⁷ is *n*-butyl.

4. The method of claim 2, wherein said ortho amino cyano aromatic compound is a compound of formula (III), R-M is benzyl magnesium halide, and R⁷ is benzyl.

5. The method of claim 2, wherein said ortho amino cyano aromatic compound is a compound of formula (III), R-M is *p*-tolyl magnesium halide, and R⁷ is *p*-tolyl.

6. The method of claim 2, wherein said ortho amino cyano aromatic compound is a compound of formula (III), R-M is 4-fluorophenyl magnesium halide, and R⁷ is 4-fluorophenyl.

7. The method of claim 2, wherein said ortho amino cyano aromatic compound is a compound of formula (III), R-M is *p*-chlorophenyl magnesium halide, and R⁷ is *p*-chlorophenyl.

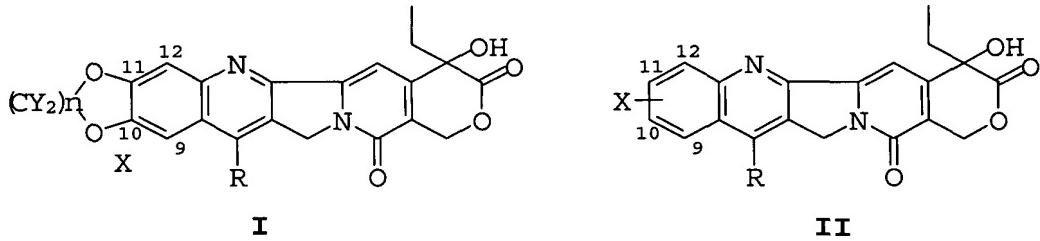
8. The method of claim 2, wherein said ortho amino cyano aromatic compound is a compound of formula (III), R-M is *p*-trifluoromethylphenyl magnesium halide, and R⁷ is *p*-trifluoromethylphenyl.

9. The method of claim 2, wherein said ortho amino cyano aromatic compound is a compound of formula (IV), R-M is *n*-butyl magnesium halide, and R⁷ is *n*-butyl.

10. The method of claim 2, wherein said ortho amino cyano aromatic compound is a compound of formula (IV), R-M is *s*-butyl magnesium halide, and R⁷ is *s*-butyl.

11. The method of claim 2, wherein said ortho amino cyano aromatic compound is a compound of formula (IV), R-M is *t*-butyl magnesium halide, and R⁷ is *t*-butyl.

12. A 7-substituted camptothecin compound of formula (I) or (II):



wherein

X is H, NH₂, H, F, Cl, Br, O-C₁₋₆ alkyl, S-C₁₋₆ alkyl, NH-C₁₋₆ alkyl, N(C₁₋₆ alkyl)₂, or C₁₋₈ alkyl,

or X is -Z-(CH₂)_a-N-(C₁₋₆ alkyl)₂ wherein Z is selected from the group consisting of O, NH and S, and a is an integer of 2 or 3,

or X is -CH₂NR²R³, where (a) R² and R³ are, independently, hydrogen, C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₃₋₇ cycloalkyl-C₁₋₆ alkyl, C₂₋₆ alkenyl, C₁₋₆ alkoxy-C₁₋₆ COR⁴ where R⁴ is hydrogen, C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₃₋₇ cycloalkyl-C₁₋₆ alkyl, C₂₋₆ alkenyl, C₁₋₆ alkoxy, C₁₋₆ alkoxy-C₁₋₆ alkyl, or (b) R² and R³ taken together with the nitrogen atom to which they are attached form a saturated 3-7 membered heterocyclic ring which may contain a O, S or NR⁵ group, where R⁵ is hydrogen, C₁₋₆ alkyl, alkyl, aryl, aryl substituted with one or more groups selected from the group consisting of C₁₋₆ alkyl, amino, C₁₋₆ alkylamino, C₁₋₆ alkoxy, C₁₋₆ alkoxy-C₁₋₆ alkyl C₁₋₆ alkyl C₁₋₆ alkoxy, aryl, and aryl substituted with one or more C₁₋₆ alkyl, or C₁₋₆ alkoxy-C₁₋₆ alkyl groups;

R is C₇₋₃₀ alkyl, substituted C₁₋₃₀ alkyl, C₁₋₃₀ alkenyl, substituted C₁₋₃₀ alkenyl, C₁₋₃₀ alkynyl, substituted , C₁₋₃₀ alkynyl, C₃₋₃₀ cycloalkyl, substituted C₃₋₃₀ cycloalkyl, C₆₋₁₈ aryl, substituted C₆₋₁₈ aryl, C₆₋₁₈ aryalkyl, (C₁₋₃₀ alkyl)₃ silyl or (C₁₋₃₀ alkyl)₃ silyl C₁₋₃₀ alkyl,

Y is independently H or F,

and

n is an integer of 1 or 2,

and salts thereof.

13. The 7-substituted camptothecin compound of claim 12, wherein R is selected from the group consisting of cyclohexyl, allyl, vinyl, 4-fluorophenyl, ethynyl, cyclopentyl, phenyl, benzyl, 1-propynyl, *p*-tolyl, *o*-tolyl, 1-trimethylsilylmethyl, hexyl, 2-thiophenyl, 4-dimethylaminophenyl, 2-(4-chloro 1-but enyl), *p*-methoxylbenzyl, methoxymethyl, *p*-chlorophenyl, *s*-butyl, *t*-butyl, and *p*-trifluoromethylphenyl.

14. The 7-substituted camptothecin compound of claim 13, wherein R is benzyl.

15. The 7-substituted camptothecin compound of claim 13, wherein R is *p*-tolyl.

16. The 7-substituted camptothecin compound of claim 13, wherein R is *p*-fluorophenyl.

17. The 7-substituted camptothecin compound of claim 13, wherein R is *p*-chlorophenyl.

18. The 7-substituted camptothecin compound of claim 13, wherein R is *p*-trifluoromethylphenyl.

19. The 7-substituted camptothecin compound of claim 13, wherein R is *s*-butyl.

20. The 7-substituted camptothecin compound of claim 13, wherein R is *t*-butyl.